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AMENDMENT	Attorney Docket Confirmation No.	CLON015
Address to: Assistant Commissioner for Patents Washington, D.C. 20231	First Named Inventor	Chenchik et al.
	Application Number	09/440,829
	Filing Date	November 15, 1999
	Group Art Unit	1655 1634
	Examiner Name	Forman, B.
	Title	Long Oligonucleotide Arrays

Sir:

This amendment is submitted in response to the Office Action dated January 8, 2002.

Please amend the above-identified application as follows:

In the Claims:

D1 2. (Amended) The array according to Claim 1, wherein two or more different target nucleic acids hybridize to different probe oligonucleotide spots in said pattern.

D2 8. (Amended) The array according to Claim 7, wherein each of said long oligonucleotide probes is cross-linked to the surface of said support at at least one site.

D3 15. (Amended) The array according to Claim 14, wherein said array comprises ten or more different probe oligonucleotide spots in said pattern, each of which hybridizes to a different target nucleic acid.

B, F & F Ref: CLON015

Clontech Ref: P-103

U.S. Application Serial No. 09/440,829

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36. (Amended) The array according to Claim 1, wherein any variance in hybridization efficiency among any two probes of said array does not exceed about 10-fold as determined using the hybridization efficiency assay described in the specification beginning at page 23, lines 4 ff.

37. (Amended) The array according to Claim 14, wherein any variance in hybridization efficiency among any two probes of said array does not exceed about 10-fold as determined using the hybridization efficiency assay described in the specification beginning at page 23, lines 4 ff.

38. (Amended) The array according to Claim 23, wherein any variance in hybridization efficiency among any two probes of said array does not exceed about 10-fold as determined using the hybridization efficiency assay described in the specification beginning at page 23, lines 4 ff.

REMARKS

In view of the above amendments and the following remarks, the Examiner is respectfully requested to withdraw the rejections and allow Claims 1-3, 7-23 and 35-38, the only claims pending and currently under examination in this application.

The Examiner is thanked for the helpful interview held on March 27, 2002 with the undersigned and Ms. Kathleen Dal Bon, in house counsel for the assignee of the above-captioned application. During this interview, the rejections made in the January 8, 2002 Office Action were discussed in view of proposed amendments. In addition, the Applicants' previously submitted declarations were discussed.

Claims 2 and 15 have been amended in accordance with the Examiner's suggestion in the Office Action. Claim 8 has been amended to correct a typographical error. Claims 36 to 38 have been amended to specify how hybridization efficiency is determined, support for this amendment being found in the specification at page 23, lines 4 ff. Attached hereto is a marked up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with markings to show changes made." As the above amendments introduce no new matter to the application, their entry by the Examiner is respectfully requested.

Claims 2-3, 15-17 and 36 to 38 were rejected under 35 U.S.C. §112, 2nd ¶ for various issues, i.e., use of the phrase "represented in" and asserted lack of essential steps, such as how hybridization efficiency is determined. In view of the above amendments to the claims where the phrase "represented in" has been removed according to the Examiner's suggestion and the manner in which hybridization efficiency is determined has been placed into the claims, this rejection may be withdrawn.

Claims 1-3, 7, 8, 10-22 and 35-37 have been rejected under 35 U.S.C. § 103(a) as assertedly being obvious over Sheiness. In making this rejection, the Examiner equates the Sheiness oligo coated beads held in a dipstick (or 96 well format) with an array, thereby concluding that the Sheiness teaches an array of oligonucleotide probes, as is claimed in the present application. The Examiner also points to the teaching of Sheiness that the probes can be 6 to 150 nt in length, and therefore concludes that Sheiness makes the claimed arrays *prima facie* obvious.

Sheiness' disclosure of probe length of 6 to 150 nt is based solely on that length being a synthesizable length. In fact, in all of the working exemplifications of Sheiness, 30-mers are employed. As such, Sheiness provides no working exemplification of the claimed narrow probe length.

Thus, the Examiner's prima facie cases of obviousness is based solely on the overlapping ranges of the claimed narrow range and the range suggested by Sheiness. The MPEP provides clear guidance as to how such a prima facie case can be rebutted. Specifically, the MPEP teaches at § 2144.05 that:

Applicants can rebut a *prima facie* case of obviousness based on overlapping ranges by showing the criticality of the claimed range. "The law is replete with cases in which the difference between the claimed invention and the prior art is some range or other variable within the claims. . . . In such a situation, the applicant must show that the particular range is critical, generally by showing that the claimed range achieves unexpected results relative to the prior art range." *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990).

As such, the claimed narrow range of probe length can render the claims patentable over Sheiness if it can be shown that the claimed probe length embodies unexpected results.

As pointed out in the Applicants' prior response, the Applicants have found unexpected results when using probes of the claimed narrow ranges, as demonstrated by the previously filed Declaration, reported in the Experimental Section of the application, and further explained in the enclosed supplemental declaration. This evidence shows that over the claimed narrow range, one unexpectedly observes a significant increase in hybridization efficiency.

In the latest office action, the Examiner discounts this previously filed declaration because it assertedly fails to provide any evidence as to why the results were unexpected. The enclosed supplemental declaration provides evidence as to what one of skill in the art would expect with respect to hybridization efficiency vs. length and therefore clearly proves that the observed results are truly unexpected.

During the above summarized interview, the Examiner also requested clarification regarding how Figure 1, which graphs signal intensity v. probe length, provides evidence of hybridization efficiency v. probe length. As explained in the enclosed supplemental declaration, signal intensity as determined using the assay reported in the application is a direct measure of hybridization efficiency. Therefore, Figure 1 clearly demonstrates the relationship of probe length and hybridization efficiency.

Thus, the experimental section of the present application clearly demonstrates that one unexpectedly obtains greater hybridization efficiency as probe length increases over the claimed probe length range. As such, the claimed range provides for unexpected results with respect to that which is suggested by the cited prior art.

Because the claimed nucleotide range clearly provides unexpected results not suggested by the broad range of Sheiness, the Examiner's *prima facie* case of obviousness is successfully rebutted by the enclosed declaration.

In sum, because Sheiness fails to suggest the narrowly claimed range of the instant application and the Applicants have demonstrated unexpected results using the claimed range, Claims 1-3, 7, 8, 10-22 and 35-38 are not obvious under 35 U.S.C. § 103(a) over Sheiness and this rejection may be withdrawn.

Claims 23 and 28 have been rejected under 35 U.S.C. §103(a) as obvious over Sheiness in view of Van Ness, for the asserted reason that Sheiness teaches all of the limitations of these claims but for the glass substrate, which the Examiner asserts is taught by Van Ness. Because Van Ness has been cited solely for the teaching of a glass support, Van Ness fails to make up the fundamental deficiencies of the primary Sheiness references as described above. Accordingly, Claims 23 and 28 are not obvious under 35 U.S.C. §103(a) over Sheiness in view of Van Ness and this rejection may be withdrawn.

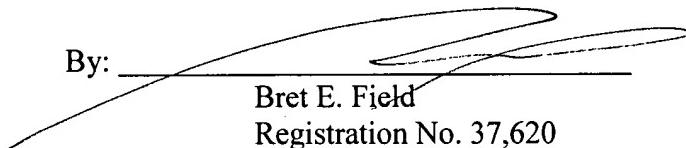
In view of the above amendments and remarks, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issuance.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815.

Respectfully submitted,

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Date: 7.3.02

By: 

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- Declaration by Alex Chenchik

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